Case Report

Acromegaly with no pituitary adenoma and no evidence of ectopic source

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ABSTRACT

More than 99% of patients with acromegaly harbor a growth hormone (GH) secreting pituitary adenoma. As the time from onset of signs/symptoms to diagnosis of acromegaly is long (symptom onset to diagnosis is often 4–10 years), pituitary adenomas that cause GH excess are often large and are nearly always visible on conventional magnetic resonance imaging (MRI). However, in rare circumstances, acromegalic patients without an ectopic source will not have imaging evidence of a pituitary adenoma. Management of these patients poses special challenge, and once ectopic source of GH/growth-hormone-releasing hormone (GHRH) is ruled out, an exploration of pituitary might be useful. We herein report a case of acromegaly with imaging evidence of sellar floor osteoma, but no pituitary adenoma, and negative work up for an ectopic source of GH/GHRH tumor, and on surgical exploration pituitary adenoma could be identified and removed and confirmed on histopathologic examination.

Key words: Acromegaly, growth hormone, magnetic resonance imaging negative, pituitary adenoma, pituitary exploration

Introduction

Acromegaly is a disorder resulting from uncontrolled hypersecretion of growth hormone (GH) and associated GH-mediated production of insulin-like growth factor 1 (IGF-1) from the liver. GH secreting pituitary adenomas are the cause of acromegaly in over 99% of patients. Most of these tumors are large and nearly always visible on magnetic resonance imaging (MRI) of the sellar region. Acromegaly secondary to a very small pituitary microadenoma not visualized on pituitary MRI is rare. There had been only three previous reports of acromegalic patients with negative pituitary imaging, in whom subsequently adenomas could be identified on pituitary exploration.

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Case Report

A 32-year-old gentleman was admitted to us with chief complaints of acral enlargement, headache and poorly controlled diabetes for last 3 years, and recently diagnosed hypertension. On examination, he had frontal bony prominence, widening of teeth spaces in lower jaw, macroglossia, and acral enlargement. His blood pressure was 140/88 mmHg on amlodepine 10 mg/day and losartan 100 mg/day. His fasting blood sugar was 160 mg/dl and glycated hemoglobin was 8.5% on glimepiride 6 mg/day and metformin 2 g/day. He was shifted to insulin and required total of 38 units insulin daily for glycemic control. With the provisional diagnosis of acromegaly further investigations were planned. Elevated serum IGF-1 levels, with unsuppressed serum GH levels (nadir serum GH level of 11.3 ng/ml) during oral glucose suppression test with 100 gram of glucose (both serum GH and IGF-1 were measured on an autoanalyzer, Roche Elecsys 2010, using electrchemiluminometric assay), confirmed the diagnosis of acromegaly. Other pituitary hormones are summarized in Table 1. For tumor localization, contrast-enhanced MRI sella with dynamic images was done,

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which showed a small nonenhancing area near to the floor of sella [Figures 1 and 2]; however, the appearance on dynamic scans was not typical for a microadenoma and hence limited computed tomography (CT) of sellar region was done which showed this lesion to be bony and arising from the floor of sella [Figure 3] and appeared as sellar floor osteoma. Subsequently, MRI with special volumetric interpolated breath-hold examination (VIBE) sequences was done, which also failed to show any pituitary adenoma. Subsequently, for ectopic source of GH secretion localization, contrast-enhanced CT scan of chest, abdomen and pelvis was done, which was normal. ^{68}Ga-DOTANOC scan also did not show any ectopic uptake. Thereafter, a decision was taken to explore the pituitary, and he underwent transnasal transsphenoidal exploration of pituitary, and a pituitary adenoma infiltrating dura could be identified and removed. Histopathologic examination of the resected lesion confirmed it as GH positive pituitary adenoma.

Table 1: Hormonal analysis of patient

Biochemical test	Results
Basal serum GH (≤1 ng/ml)	31.8
Post glucose suppressed serum GH (≤1 ng/ml)	11.3
Serum IGF-1 (ng/ml)	1512
Serum total T4 (5.1–14.1 μg/dl)	8.33
Serum TSH* (0.27–4.2 μIU/ml)	1.12
8 AM serum cortisol (6.2–19.4 μg/dl)	20.96
Plasma ACTH† (7.2–63.3 pg/ml)	21.13
Serum LH‡ (1.7–8.6 mIU/ml)	1.9
Serum FSH§ (1.5–12.4 mIU/ml)	3.5
Serum testosterone(2.4–8.3 ng/ml)	1.11
Serum prolactin (4.6–21.4 ng/ml)	7.11

*TSH: Thyroid stimulating hormone, †Adrenocorticotropic hormone, ‡Luteinizing hormone, §Follicle-stimulating hormone, GH: Growth hormone, IGF-1: Insulin-like growth factor 1, ACTH: Adrenocorticotropic hormone, LH: Luteinizing hormone, FSH: Follicle stimulating hormone

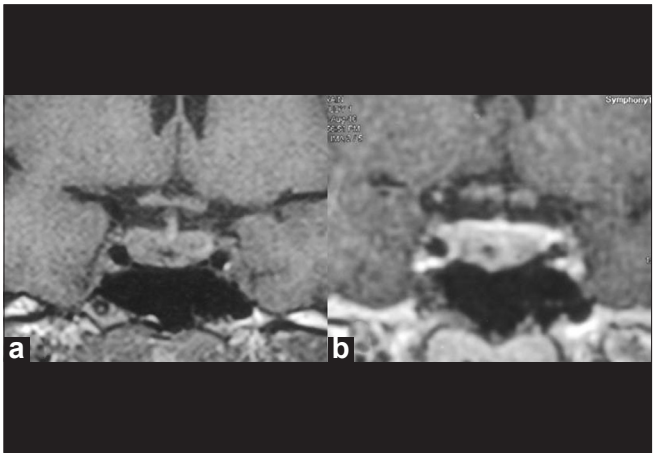

Figure 2: T1-weighted coronal MR image (a) pre-contrast and (b) post-contrast shows the same lesion with no enhancement

Discussion

Acromegaly is a disorder resulting from uncontrolled hypersecretion of GH and associated GH-mediated production of IGF-1 from the liver. The elevated GH and IGF-I levels in acromegaly lead to a wide range of cardiovascular, respiratory, endocrine, and metabolic morbidities.[1] The clinical manifestations range from subtle signs of acral overgrowth, soft-tissue swelling, arthralgias, jaw prognathism, fasting hyperglycemia, and hyperhidrosis to florid osteoarthritis, frontal bone bossing, diabetes mellitus, hypertension, and respiratory and cardiac failure.[2] The diagnosis of acromegaly is frequently delayed due to its indolent and insidious nature. However, untreated acromegaly is associated with a significant morbidity and a reduced life expectancy.[3] GH secreting pituitary adenomas are the cause of acromegaly in over 99% of patients.[4] So,

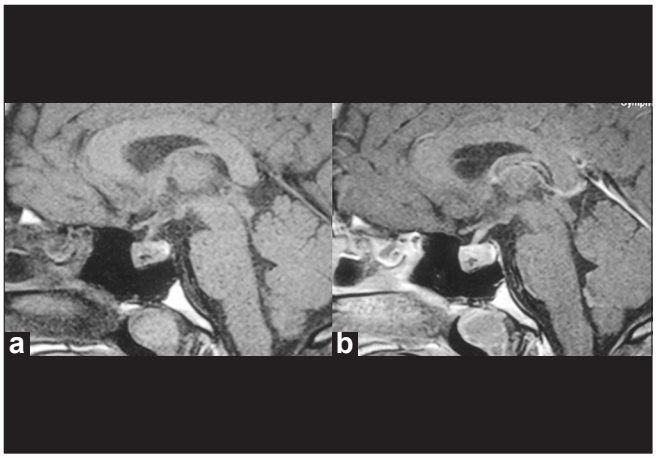

Figure 1: T1-weighted sagittal MRI image (a) shows a small hypointense area in the anterior pituitary which has the same appearance on post-contrast image (b)

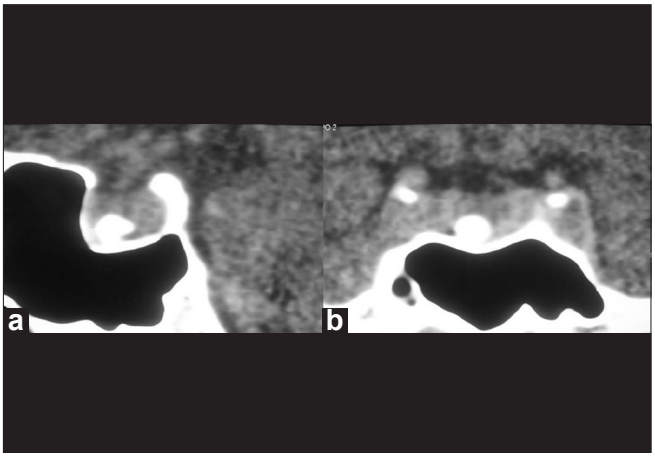

Figure 3: CT sella of the same patient, sagittal reformatted image (a) and coronal reformatted image (b) showing the lesion to be bony and arising from the floor of sella

once biochemical diagnosis of acromegaly is confirmed, pituitary MRI is the first step in localizing the GH excess. Adenomas precipitating acromegaly are usually more than 1 cm in diameter at the time of diagnosis and nearly always visible on conventional MRI. Other rare causes of acromegaly include pituitary somatotroph carcinomas, hypothalamic tumors secreting growth-hormone-releasing hormone (GHRH), and a nonendocrine tumors causing ectopic secretion of GH or GHRH. So, if pituitary MRI is unremarkable, contrast-enhanced CT scan of chest, abdomen and pelvis is the next step to look for ectopic source of GH/GHRH.[5]

Acromegaly secondary to a very small pituitary microadenoma not visualized on pituitary MRI is rare. To the best of our knowledge, previously there had been only three reports of acromegalic patients with negative pituitary imaging, in whom subsequently adenomas could be identified on pituitary exploration. Doppman *et al*.[6] described three acromegalic patients in whom MRI imaging failed to detect a pituitary adenoma that was later discovered at surgery (resected adenoma sizes: 6, 7, and 10 mm, respectively). However, only one of their patients underwent a contrast-enhanced MRI study. The other two patients had only noncontrast MRI imaging, which may not be a sensitive imaging for small adenomas. Daud *et al*.[7] reported an acromegalic patient who did not have imaging evidence of a pituitary adenoma with contrast-enhanced MRI, including thin-cut spoiled-gradient recalled (SPGR) imaging. Surgical exploration revealed 9-mm adenoma and was successfully removed. Lonser *et al*.[8] recently reported a series of six acromegalic patients without imaging evidence of pituitary adenoma on conventional contrast-enhanced MRI, who also lack an ectopic source. Subsequently, postcontrast fine-cut VIBE MRI sequence revealed a 4-mm pituitary adenoma in one out of three patients, who had this special MRI sequence imaging. However, on surgical exploration, pituitary microadenomas could be identified in all cases.

In our case, imaging with conventional MRI (1.5 T magnet), followed by a second, fine-cut VIBE sequence, failed to reveal a pituitary adenoma. However, on surgical exploration, a pituitary adenoma infiltrating dura could be identified and removed. To rule out an ectopic source of GH/GHRH, we had done contrast-enhanced CT scan of chest, abdomen and pelvis, as well as nuclear imaging ^{68}Ga-DOTANOC, both of which did not show any ectopic source. Currently, there is no consensus for the treatment of patients with acromegaly and negative pituitary imaging.[9] Medical therapy is one of the other treatment options in these patients; however, our patient was not able to afford long-term medical treatment and opted for surgical exploration after discussion. Finding of sellar floor osteoma in our patient is unusual. Previously, there had been few case reports[10,11,12] of osteoma in association with acromegaly and in one of the cases, even progression of osteoma related to acromegaly.[12]

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